

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	09/844353	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/08 12:20
L2	28	Ruvkun NEAR Gary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/08 12:20
L3	4119	AKT AKT-1 AKT-2 AKT-\$1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/08 12:23
L4	87792	insulin	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2007/05/08 12:23
L5	10337	ELEGANS	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/05/08 12:23
L7	223	I3 I4 I5	US-PGPUB; USPAT; EPO; JPO; DERWENT	AND	ON	2007/05/08 12:27
L9	27	I3 I4 I5	US-PGPUB; USPAT; EPO; JPO; DERWENT	SAME	ON	2007/05/08 12:29
L10	4	(I3 I4 I5).clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	AND	ON	2007/05/08 12:29

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(FILE 'HOME' ENTERED AT 12:09:32 ON 08 MAY 2007)

FILE 'MEDLINE, SCISEARCH, CAPLUS, BIOSIS' ENTERED AT 12:09:56 ON 08 MAY 2007

L1 55181 S AKT OR AKT-1 OR AKT-2
L2 889411 S INSULIN
L3 77764 S ELEGANS
L4 131 S L1 (L) L2 (L) L3
L5 46 DUP REM L4 (85 DUPLICATES REMOVED)
L6 0 S L5 AND PY<=1997
L7 131 FOCUS L4 1-
L8 46 FOCUS L5 1-
E RUVKUN GARY?/AU
L9 16 S E1
E RUVKUN G?/AU
L10 195 S E1
E OGG SCOTT?/AU
L11 20 S E2
L12 231 S L9 OR L10 OR L11
L13 16 S L12 AND L4
L14 7 DUP REM L13 (9 DUPLICATES REMOVED)
L15 7 SORT L14 PY

=> d ti so au ab pi l15 7 4 2

L15 ANSWER 7 OF 7 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on
STN
TI Two membrane-associated tyrosine phosphatase homologs potentiate C-elegans
AKT-1/PKB signaling
SO PLOS GENETICS, (JUL 2006) Vol. 2, No. 7, arn. e99.
ISSN: 1553-7390.
AU Hu P J; Xu J L; Ruvkun G (Reprint)
AB **Akt**/protein kinase B (PKB) functions in conserved signaling
cascades that regulate growth and metabolism. In humans, **Akt**
/PKB is dysregulated in diabetes and cancer; in *Caenorhabditis*
elegans, **Akt**/PKB functions in an **insulin**-like
signaling pathway to regulate larval development. To identify molecules
that modulate C. **elegans** **Akt**/PKB signaling, we
performed a genetic screen for enhancers of the **akt-1**
mutant phenotype (eak). We report the analysis of three eak genes. eak-6
and eak-5/sdf-9 encode protein tyrosine phosphatase homologs; eak-4
encodes a novel protein with an N-myristoylation signal. All three genes
are expressed primarily in the two endocrine XXX cells, and their
predicted gene products localize to the plasma membrane. Genetic evidence
indicates that these proteins function in parallel to **AKT**-
1 to inhibit the FoxO transcription factor DAF-16. These results
define two membrane-associated protein tyrosine phosphatase homologs that
may potentiate C. **elegans** **Akt**/PKB signaling by cell
autonomous and cell nonautonomous mechanisms. Similar molecules may
modulate **Akt**/PKB signaling in human endocrine tissues.

L15 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
TI Genes and polypeptides involved in insulin signaling pathways for glucose
tolerance, obesity, and longevity and their uses as therapeutic and
diagnostic tools
SO PCT Int. Appl., 402 pp.
CODEN: PIXXD2
IN Ruvkun, Gary; Ogg, Scott
AB Disclosed herein are novel genes and methods for the screening of
therapeutics useful for treating impaired glucose tolerance conditions, as
well as diagnostics and therapeutic compns. for identifying or treating

such conditions. The *Caenorhabditis elegans* metabolic regulatory genes *daf-2* and *age-1* encode homologs of the mammalian **insulin** receptor/phosphoinositol 3-kinase signaling pathway proteins, resp. Also, the *C. elegans* PKB kinase and **AKT** kinase act downstream of these genes, as their mammalian homologs act downstream of **insulin** signaling. The *C. elegans* PTEN lipid phosphatase homolog, *DAF-18*, acts upstream of **AKT** in this signaling pathway. Further, the *DAF-16* forkhead protein represents the major transcriptional output of this **insulin** signaling pathway. Addnl. evidence indicates that the *DAF-16*, *DAF-3*, *DAF-8*, and *DAF-14* transcriptional outputs of converging signaling pathways regulate metabolism. The congruence between the *C. elegans* and mammalian **insulin** signaling pathways strongly supports the contention that new genes identified in the *C. elegans* pathway also act in mammalian **insulin** signaling. Exemplary sequences and functional characteristics of the *C. elegans* *daf* genes and their human homologs are provided.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000033068	A1	20000608	WO 1999-US28529	19991202
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001029617	A1	20011011	US 1998-205658	19981203
US 6861256	B2	20050301		
AU 2000017496	A	20000619	AU 2000-17496	19991202
EP 1163515	A1	20011219	EP 1999-960641	19991202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

L15 ANSWER 2 OF 7 MEDLINE on STN

TI *Caenorhabditis elegans* Akt/PKB transduces **insulin** receptor-like signals from AGE-1 PI3 kinase to the *DAF-16* transcription factor.

SO Genes & development, (1998 Aug 15) Vol. 12, No. 16, pp. 2488-98.
Journal code: 8711660. ISSN: 0890-9369.

AU Paradis S; Ruvkun G

AB A neurosecretory pathway regulates a reversible developmental arrest and metabolic shift at the *Caenorhabditis elegans* dauer larval stage. Defects in an **insulin**-like signaling pathway cause arrest at the dauer stage. We show here that two *C. elegans* **Akt**/PKB homologs, *akt-1* and *akt-2*, transduce **insulin** receptor-like signals that inhibit dauer arrest and that **AKT-1** and **AKT-2** signaling are indispensable for **insulin** receptor-like signaling in *C. elegans*. A loss-of-function mutation in the Fork head transcription factor *DAF-16* relieves the requirement for **Akt**/PKB signaling, which indicates that **AKT-1** and **AKT-2** function primarily to antagonize *DAF-16*. This is the first evidence that the major target of **Akt**/PKB signaling is a transcription factor. An activating mutation in *akt-1*, revealed by a genetic screen, as well as increased dosage of wild-type *akt-1* relieves the requirement for signaling from AGE-1 PI3K, which acts downstream of the *DAF-2* **insulin**/IGF-1 receptor homolog. This demonstrates that **Akt**/PKB activity is not necessarily dependent on AGE-1 PI3K activity. *akt-1* and *akt-2* are expressed in overlapping patterns in the nervous system and in tissues that are remodeled during dauer formation.

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☐ **1: [AAE68981](#). Reports Sequence 87 from ...[gi:15113397]**

[BLink](#), [Links](#)

>gi|15113397|gb|AAE68981.1| Sequence 87 from patent US 6225120

[Next sequence](#)

EVLEDNDYGRAVDWWGLGVVMYEMMCGRLPFYNDHEKLFELILMEEIRFPRTLGPAAKSLLSGLLKKDP
 TQRLGGGSEDAKEIMQHRFFANIVWQDVYEKKLSPFPKPQVTSETDTRYFD

☐ **2: [AAE68983](#). Reports Sequence 89 from ...[gi:15113399]**

[BLink](#), [Links](#)

>gi|15113399|gb|AAE68983.1| Sequence 89 from patent US 6225120

[Previous sequence](#)
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TMNEFEYLKLLGKGTFGKVILVKEKATGRYYAMKILKKEVIVAKDEVAHTLTENRVLQNSRHPFLT

☐ **3: [AAE68985](#). Reports Sequence 91 from ...[gi:15113401]**

[BLink](#), [Links](#)

>gi|15113401|gb|AAE68985.1| Sequence 91 from patent US 6225120

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KLENLMLDKDGHKITDFGLCKEGIKDGATMKTFCGTPEYLAPEV

☐ **4: [AAE68987](#). Reports Sequence 93 from ...[gi:15113403]**

[BLink](#), [Links](#)

>gi|15113403|gb|AAE68987.1| Sequence 93 from patent US 6225120

[Previous sequence](#)
[Next sequence](#)

FLTALKYSFQTHDRLCFVMEYANGGELFFHLSRERVFSEDRARFYGAIEVSALDYLH

☐ **5: [AAE68989](#). Reports Sequence 95 from ...[gi:15113405]**

[BLink](#), [Links](#)

>gi|15113405|gb|AAE68989.1| Sequence 95 from patent US 6225120

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[Next sequence](#)

NNFSVAQCQLMKTERPRPNTFIIRCLQWTTVIERTFHVETPEEREWATAIQTVADGLK

☐ **6: [AAE68991](#). Reports Sequence 97 from ...[gi:15113407]**

[BLink](#), [Links](#)

>gi|15113407|gb|AAE68991.1| Sequence 97 from patent US 6225120

[Previous sequence](#)

LTALKYSFQTHDRLCFVMEYANGGELFFHLSRE